SPECIFICATION AMENDMENTS

Please amend the above-identified application as follows.

Please amend the title to read as follows:

"COMPOSITION AND METHOD FOR INCREASING EXORPHIN CATABOLISM TO TREAT AUTISM".

Please amend the paragraph on page 1, lines 14-19, as follows:

B1

The present invention relates to treating autism and, more specifically, to treating autism ~~with genomeceutical based treatments~~ by increasing expression and/or activity of exorphin cleaving gene products. The present invention also includes the use of phytase and like substances and formulations containing ~~one or more of genomeceutical,~~ enzymatic and phytase-like compounds for treating autism.

Please amend the paragraph on pages 4-5, lines 25-9, as follows:

B2

To compensate for the apparent lack of sufficient quantities of DPPIV and to generally rebuild proper functioning of an autistic individual's intestinal tract with regard to absorption and digestion, different approaches have been employed. Of these, enzyme therapy and probiotic supplementation have been favored and met a degree of success. Enzyme therapy has typically been based on supplementation with large amounts of proteases from ~~the~~ different categories of proteolytic enzymes and these have included acid or carboxyl peptidases, peptidases with both endo- and exo-peptidase activity, and serine, ~~cystein~~ cysteine and zinc proteases. More recently, exogenic DPPIV from animal (usually cow or pig) and plant sources has been utilized (see *Peptidase Enzyme Digestive Aid Project*, by Pangborn, J., published at the Autism Research Institute's 3rd Annual Defeat Autism Now! Conference, September, 1997). While enzyme therapy has had limited success, it is disadvantageous, amongst other reasons, in that many proteases, including DPPIV, are broken down in the stomach and do not reach the intestines in a functional state.

Please amend the paragraph on page 6, lines 8-19, as follows:

It is another object of the present invention to utilize ~~genomeceutical~~ ingestible materials that modify expression of DPPIV, QPP or another compound whose regulation is beneficial in treating autism.

It is another object of the present invention to provide various formulations that include ~~genomeceutical~~ material that affects the expression or activity of a gene product useful in treating autism and one or more proteases/peptidases for treating autism.

B3

It is also an object of the present invention to provide various formulations for treating autism that include phytase (or phytase-like substances) and protease and/or ~~genomeceutical~~ material that affects the expression or activity of a gene product useful in treating autism.

Please amend the paragraphs on page 7, lines 2-30, as follows:

~~Genomeceuticals (GCs)~~ There are ~~naturally occurring~~ compounds or materials that when ingested can cause a gene to either alter its expression pattern (i.e., make more or less of ~~the~~ its product), affect the fidelity of a gene (i.e., how well that gene product works) or affect the integrity of a gene (i.e., whether or not the gene is functional). ~~GCs~~ These gene product affecting materials do not directly replace substances that are missing (e.g., an enzyme diminished by mutation), but actually alter the expression and/or functionality of the gene products.

B4

Glucosamine is an example of ~~a GC~~ such a material. Glucosamine has been shown to increase the level of transcription and translation of important genes. Adding glucosamine to a diet has been shown to increase both RNA and protein levels. The addition of glucosamine also increases the expression of leptin (a fat hormone), again suggesting an expression based response to the presence of glucosamine.

The present invention provides the novel approach of utilizing ~~GCs~~ ingestible gene product affecting materials to treat autism. For example, in at least one embodiment discussed below, the present invention includes the use of the milk sugar galactose to modify (e.g., up regulate) DPPIV expression. This up regulation may occur in cells within the intestinal tract and possibly elsewhere. Although not concerned with autism, Smith et al have reported that galactose can increase the expression of DPPIV in cultured mouse intestinal wall cells (also known as enterocyte cells). (see Smith,M.W., James,P.S., Peacock,M.A., *Galactose Effects on Enterocyte Differentiation in the Mouse Jejunum.* Biochem Biophys Acta Jul. 10, 1991, 1093(2-3):1446).

Please amend the paragraphs on page 8, lines 7-24, as follows:

In addition to galactose, the present invention may also include the use of other ~~GCs~~ gene product affecting materials, various proteases and/or peptidases, compounds that increase up take of substances that facilitate gene expression, phospholipids, disacchradases, lipases, related compounds and combinations of these items. Various representative, but not exclusive, embodiments of the present invention are now discussed in more detail.

Formulation A

In one embodiment of the present invention, termed formulation A for purposes of the present discussion, galactose is provided ~~as a genomeceutical~~ to increase expression of DPPIV. The galactose is preferably combined with other substances to enhance overall effectiveness. The other substances in the preferred embodiment of formulation A include: acid fast protease (AFP); bromelain and/or papain; peptidase concentrate; lactase and phytase.

Please amend the paragraph on pages 9, lines 19-26, as follows:

To further assist with this digestion a ~~cystein~~ cysteine protease is preferably used. Bromelain and papain are examples of a ~~cystein~~ cysteine protease. Bromelain is preferred over papain because research has suggested that bromelain has a wider specificity and function than papain. It has also been demonstrated that bromelain is an effective anti-inflammatory which may be significant in reducing the "leaky gut" characteristic of autistic individuals.

B6

Please amend the paragraph on pages 9-10, lines 27-2, as follows:

A peptidase concentrate component is preferably provided that exhibits endo- and exo-peptidase activity. It is further preferred that the peptidase concentrate mimics DPPIV activity and hence provides further exorphin digestion. A suitable peptidase concentrate, amongst others, is the Case-Glutenase concentrate available commercially from Kirkman Laboratories in ~~Wilsonville~~Lake Oswego, OR.

B7

Please amend the paragraph on page 11, lines 18-24, as follows:

The functioning of galactose is believed to be at at least two levels. A first level is ~~as a genomeceutical where it is believed to be~~ increasing the gut expression of the DPPIV gene. This increased expression allows for a greater level of the DPPIV enzyme in human enterocytes and other cells which in turn achieves a more thorough breakdown of any exorphins.

B8

Please amend the paragraph on pages 12-13, lines 18-2, as follows:

It should be recognized that while Formulation A preferably has at least the listed six ingredients, the present invention may include combinations of less than all of the listed ingredients, as determined by the limits of prior art. For example, the combination of ~~a GC~~ an ingestible gene product affecting material for treating autism and proteases/peptidase is within the present invention as is the combination of ~~a GC for~~

B9

~~treating autism~~ such an ingestible gene product affecting material and phytase or a phytase like compound. If a patient does not have milk in their diet or is not lactose intolerant then lactase may not be necessary. Further variations are suggested elsewhere herein and others yet would be apparent to skilled practitioners given the teachings herein. Given the exponential combination of ingredients all variations are not specifically called out, though it should be recognized that they are intended to fall within the present invention.

Please amend the paragraph on page 14, lines 13-28, as follows:

When macrophages are exposed to beta glucans, such as the yeast cell wall beta-1,3/1,6-glucan, they become non-specifically stimulated so that subsequent antigen exposure results in a much more robust immune response than would otherwise happen. Among those responses is the secretion of cytokines and the processing and subsequent presentation of antigens to T-cells. The role of antigen presentation is accomplished through interaction with the TCR. The bound TCR then transduces a signal to the nucleus directing an altered expression pattern which includes modified expression of available QPP. QPP is then secreted into circulation and is free to digest any exorphins present. Glucans have also been shown to up-regulate transcription factors in the cell nucleus. Hence, glucans can serve as ~~a genomeceuticalan~~ ingestible material for increasing expression of QPP.

Please amend the paragraph on page 15, lines 1-13, as follows:

Other ~~Genomeceuticals~~Materials/Sugars

Lactose, fructose, sucrose, glucose, etc., are sugars that may be present in milk, as is galactose. The presence of one or more of these sugars may cause the intestinal cells to produce enzymes, including DPPIV like enzymes, that are effective in breaking down milk proteins and milk protein by-products (such as exorphins, amongst others). Thus, while galactose is a preferred

sugar, it is possible that one or more of these other sugars and/or related compounds may exhibit efficiency in promoting expression of DPPIV like enzymes. Furthermore, the provision of lactose and lactase would provide galactose as a by-product.

B1 Out

Please amend the paragraph on page 16, lines 1-5, as follows:

Phytase

In addition to Formulation A, the present invention includes both (1) the combination of phytase and ~~a genomeceutical~~ an ingestible material that affects endogenously produced gene products for treating autism and (2) the combination of phytase and a protease and/or peptidase for treating autism.

B2

Please amend the paragraph on pages 16-17, lines 29-2, as follows:

Lipase and Other Enzymes

Lipase, amylase and other related enzymes may also be provided in accordance with the present invention. Amylase liberates glucose from carbohydrates, and the liberated carbohydrate may serve as a ~~genomeceutical~~ material that positively affects an endogenously produced gene product as discussed above. A fungal based amylase is available commercially. Other amylases may also be suitable.

B3